United States Department of Health and Human Services

Office of the Assistant Secretary for Preparedness and Response

Project BioShield Annual Report to Congress

January 2012 – December 2012

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Foreword

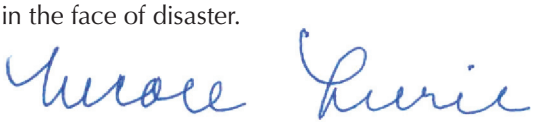
The Medical Countermeasures (MCM) Enterprise had a significant year in 2012. The U.S. Department of Health and Human Services' (HHS) continued to leverage recommendations of the "Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs" (MCM Review), released in August 2010, to foster and promote capabilities to prepare and respond to a wide range of threats while balancing limited resources.

The Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) coordinates federal efforts to enhance chemical, biological, radiological, and nuclear threats, and emerging infectious disease preparedness. To improve transparency and strengthen the decision-making process of the PHEMCE, the MCM Review recommended HHS establish an improved, formal governance structure to oversee and serve as the decision forum for MCM investment and policies. Since it was chartered in 2012, the Enterprise Senior Council – which includes representatives from the Centers for Disease Control and Prevention, the Food and Drug Administration, the National Institutes of Health, as well as several interagency partners, including the Departments of Defense, Veterans Affairs, and Homeland Security – has reviewed acquisitions, investments, and changes in policies related to MCMs. Guiding these efforts moving forward, the *HHS Public Health Emergency Medical Countermeasures (PHEMCE) Strategy* and *Implementation Plan*, both released in 2012, identify, describe, and guide prioritization of MCM development, procurement, distribution, utilization planning, and distribution in the near-, mid-, and long-term, including through the use of the Project BioShield Special Reserve Fund.

A critical priority of the MCM Enterprise is the capability to rapidly manufacture needed products to limit the adverse health impacts of a public health emergency. When the MCM Review was released in 2010, the nation's domestic manufacturing capacity was limited. Since that time, HHS has prioritized investment in flexible, platform-based manufacturing capabilities that allow us to respond to a range of threats more quickly. For example, in an emergency we would be able to switch from making pandemic influenza vaccine to making a MCM to treat the effects of a chemical, biological, radiological, or nuclear agent. A significant step forward in fostering this technology was an award in 2012 to establish the Centers for Innovation in Advanced Development and Manufacturing. Once complete, these Centers will have multiple functions, including: assisting developers in product development and manufacturing; expanding domestic manufacturing surge capacity; and providing workforce development training. These Centers will expand our readiness to respond quickly to a number of public health emergencies and will reduce dependence on off-shore manufacturing.

HHS has made significant progress in implementing the recommendations of the MCM Review to support a forward-looking MCM Enterprise that is flexible and adaptable. As HHS has implemented these initiatives, gaps were identified in existing authorities and changes in policies were highlighted that would be beneficial to the success of the MCM Enterprise. HHS was able to work closely with congressional colleagues throughout 2012 and on March 13, 2013, President Obama signed the Pandemic and All-Hazards Preparedness Reauthorization Act into law. This legislation strengthens existing authorities; requires development of the next iteration of the National Health Security Strategy; directs a coordinated approach to preparedness grants; clarifies and enhances the Food and Drug Administration's Emergency Use Authorization authorities for MCMs; and, reauthorizes a number of our core programs, including reauthorization of the Special Reserve Fund that supports Project BioShield acquisitions through 2018. As required by PAHPRA, HHS will include the information from this report in subsequent submissions of the PHEMCE Strategy and Implementation Plan.

Progress over the past ten years, both within the MCM Enterprise and in the Project BioShield program, has been substantial. Success was in large part a result of partnership and collaboration among public agencies and the private sector. With the continued dedication of our partners, our national health security will continue to improve and our communities will become more resilient in the face of disaster.



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1.0 PROJECT BIOSHIELD AUTHORITIES & REPORTING REQUIREMENTS

THE PROJECT BIOSHIELD ACT OF 2004 (Public Law [P.L.] 108-276) was designed to provide additional and more flexible authorities and funding to support financially the development and procurement of medical countermeasures against chemical, biological, radiological, and nuclear (CBRN) threat agents, referred to as the Project BioShield Program (PBS). The Project BioShield Act was also designed to provide the government with the authority to quickly authorize their use during emergencies. These authorities were further delineated, clarified, expanded, and extended by the Pandemic and All-Hazards Preparedness Act of 2006, P.L. 109-417, the legislation that authorized the establishment of the Biomedical Advanced Research and Development Authority (BARDA) within the U.S. Department of Health and Human Services (HHS). These authorities were further refined, extended, and expanded under the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, P.L. 113-5 (PAHPRA), which reauthorized the Special Reserve Fund and expanded the Secretary's authorities to permit use of unapproved products or unapproved uses of approved products during emergencies.[1]

The Public Health Service Act (the Act), as amended by the Project BioShield Act, PAHPA, and PAHPRA, requires the Secretary of HHS (the Secretary) to submit to Congress an annual report describing the use of specific provisions within the following authorities:

- **Research and Development of Qualified Medical Countermeasures** – Section 2 of the Act authorizes the use of a variety of streamlined procedures in awarding grants, contracts, and cooperative agreements relating to the research and development of qualified countermeasures. Reporting is required on the use of limited competition, expedited peer review, and increased simplified acquisition thresholds.
- **Security Countermeasure Procurements and Special Reserve Fund** – Section 3 of the Act authorizes the appropriation of up to $5.593 billion over the period of fiscal year FY 2004 through FY 2013 in a Special Reserve Fund (SRF) for the procurement of security countermeasures for the Strategic National Stockpile (SNS or the stockpile). The Act specifies that up to $3.4 billion could be obligated from FY 2004 through FY 2008, with the balance available from FY 2009 through FY 2013. Furthermore, it also authorizes the use and reporting of simplified acquisition procedures, the modified use of other than full and open competition, and the payment of premiums in multiple-award contracts.

- **Emergency Use Authorization for Medical Countermeasures** – Section 4 of the Act allows the HHS Secretary to issue an Emergency Use Authorization (EUA) after an emergency has been declared by the Secretary as described in the "Statutory Authority" section found on page 7. The EUA declaration justifies the use of a FDA-approved, licensed, or cleared product for an unapproved indication or an unapproved product for an indication over a specified period of time during the emergency. The HHS Secretary has delegated the authority to issue an EUA to the FDA Commissioner. Reporting is required on emergency uses of certain biologicals, drugs and devices, emergency declarations, and conditions of authorization.

[1]The Pandemic and All-Hazards Preparedness Act of 2013 (PAHPRA), which was enacted on March 13, 2013 (Pub. L. 113-5, 127 Stat. 161) amended Section 2811 of the Public Health Service Act (42 U.S.C. 300hh–10) requiring HHS to include information formerly submitted as the Project BioShield Report in submissions of the PHEMCE Strategy and Implementation Plan. Future reports will include PBS information with the PHEMCE Strategy and Implementation Plan. PAHPRA also reauthorizes the Special Reserve Fund under Section 319F–2 of the Public Health Service Act (42 U.S.C. 247d–6b) and amends and adds to the Emergency Use Authority under Section 564 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–3).

Specifically, the Act requires the annual report to include the following information for each use of the specific provisions within the following authorities:

- The particular actions taken under each authority, including the identification of the threat agent, emergency, or medical countermeasure;
- The reasons underlying each action, including, if applicable, a description of options considered for each action;
- The number and nature of entities that received or were denied a grant, cooperative agreement, or contract; and
- Whether each countermeasure acquisition that required presidential approval resulted in a contract that was entered into within one year of such approval (the President has delegated the authority to approve acquisitions to the Director of the Office of Management and Budget [OMB]).

The Act also requires a separate summary of National Institutes of Health (NIH) activities related to the use of funds for research and development of (a) the increased micro-purchase threshold, (b) authority for personal services contracts, and (c) streamlined personnel authority for NIH positions.

1.1 AUTHORITY USAGE

In 2012, HHS used two of the Act's authorities that require annual reporting on the procurement of security countermeasures and issuance of EUAs. HHS did not utilize the additional authorities of expedited peer review authority, simplified acquisition procedures, or premium provision in multiple-award contracts. The standard Federal Acquisition Regulation (FAR) practices were deemed adequate for all acquisition activity during the 2012 reporting period.

1.2 EXPEDITED PEER REVIEW

The National Institute of Allergy and Infectious Diseases (NIAID) within the NIH did not use its expedited peer review authority during the 2012 reporting period.

1.3 SECURITY COUNTERMEASURE PROCUREMENT

Through BARDA, HHS provided additional funds ($62M) (**Table 1**) to further support three programs that are currently funded under PBS. The 2012 PBS strategy included support of pivotal studies on medical countermeasures (MCMs) procured previously under PBS and delivered to the SNS that enable product licensure or approval, replenishment of expiring unlicensed MCMs procured under PBS and delivered to the SNS, and procurement of new MCMs. Funds were approved and obligated on existing MCM projects for the first element of this strategy, and solicitations (or Request for Proposals – RFPs) were issued for the latter two elements of the strategy with the expectation of making contract awards by the end of FY 2013.

In April and September 2012, BARDA provided $32M and $5M, respectively, to Bavarian Nordic. Bavarian Nordic is developing a smallpox vaccine for "at-risk" populations and has been delivering their vaccine, IMVAMUNE®, to the stockpile since early 2010. The FDA requested that the proposed Phase 3 human clinical study be modified to provide evidence of effectiveness when compared to the approved smallpox vaccine, ACAM2000. The additional funds supported an expanded pivotal Phase 3 clinical study deemed essential for licensure of the vaccine. In September, $5M was provided to support studies to evaluate the stability of the bulk drug substance stored for long periods (in excess of 2 years). The results of these studies will inform the feasibility of a transition strategy to move from the current liquid vaccine formulation to a more cost effective freeze-dried formulation. The same bulk drug substance will be used to formulate both the current liquid formulation and the more cost-effective lyophilized final drug products later this decade. Further, these studies may afford the stockpiling of bulk vaccine antigen for this product at a domestic fill-finish manufacturing site as an intermediate similar to the strategy used successfully by BARDA for pre-pandemic H5N1 influenza vaccine and adjuvants since 2004. Additionally, in January 2012, the current EUA submission on file with the FDA was extended to include individuals with atopic dermatitis in addition to the current use in those individuals infected with the human immunodeficiency virus (HIV). This smallpox vaccine product may be authorized for use in both special populations of all age ranges, and in pregnant and nursing mothers afflicted with either condition in the event of a declared smallpox emergency.

In April 2012, $8.7M was added to the PBS project with Emergent BioSolutions for further late stage development and procurement of their anthrax vaccine BioThrax®

In addition to the pivotal Phase 3 clinical safety study to support licensure for post-exposure prophylaxis, the FDA asked if a bi-directional study to evaluate the effect of ciprofloxacin on the immune response had been considered. The additional funds supported this study, which will complement another pivotal clinical study already completed for a Biological License Application submission to the FDA for this indication.

In April 2012, $16.6M was added to the current PBS project with Cangene for further late stage development and procurement of their polyclonal anthrax antitoxin (AIG). Based on discussions between the FDA and the licensing pathway for anther anthrax antitoxin (i.e., Raxibacumab® from Human Genome Sciences/GlaxoSmithKline), added benefit studies were implemented for the Cangene antitoxin product. The added benefit studies were designed to show how much more effective a treatment regimen involving both antibiotics and this antitoxin are than antibiotics alone against inhalational anthrax in an animal challenge model. The modest additional investment on the Cangene project ensured better probability of final licensure success.

A major milestone was realized in the PBS program in December 2012 with the FDA approval of Raxibacumab® anthrax antitoxin. This approval represented the first biological product licensed under the FDA's "Animal Efficacy Rule" and the first product supported solely by PBS to attain licensure/approval status. Additionally, this action affirmed the BARDA strategy supporting the advanced development of CBRN MCMs towards product licensure.

BARDA issued four solicitations in 2012 to support the development of CBRN MCMS and to develop and procure existing and new medical countermeasures under PBS (**Table 2**). In June 2012, BARDA issued its third Broad Agency Announcement seeking proposals for the development of medical countermeasures to treat, prevent, or diagnose the medical consequences of CBRN attacks. Proposals were received and evaluated, and contract awards were announced in 2012 for multiple new product candidates in the areas of broad spectrum antimicrobials, cell therapies and small molecule drugs for the treatment of Acute Radiation Syndrome (ARS) illnesses including thermal burns and chemical decontamination. HHS provided funds in 2012 for BARDA Advanced Research and Development (ARD) programs for these new MCM candidates, as well as for existing projects on the development of anthrax vaccines and antitoxins, smallpox vaccines and antiviral drugs, broad spectrum antibiotics, biothreat diagnostics, ARS treatments, biodosimetry devices, and chemical antidotes.

In June 2012, BARDA issued a solicitation to purchase anthrax antitoxins for the treatment of inhalational anthrax with antibiotics. An analysis of the existing SNS inventory of unlicensed anthrax antitoxins showed that the potency of the product would render the stockpile obsolete without replenishment. This solicitation was issued to replenish the stockpile at current levels through the latter part of this decade and to acquire hybridoma cell lines expressing anthrax antitoxin antibodies for future production if needed in an emergency. Proposals were received and reviewed by BARDA, and contract negotiations were on-going at the end of 2012.

In June 2012, BARDA issued a solicitation to purchase anti-neutropenia cytokines for treatment of hematopoietic illnesses associated with ARS in affected individuals following a radiation event. The changes in the business model for marketing these cytokines commercially and the FDA acceptance of the data to support a pre-EUA for Neupogen® (Amgen) informed the feasibility of this solicitation. BARDA received and reviewed proposals for these medical countermeasures, which would be stored under vendor-managed inventory systems, and contract negotiations were on-going at the end of 2012.

In November 2012, BARDA issued a solicitation to purchase the anti-convulsive drug Midazolam for treatment of individuals exposed to highly volatile nerve agents. The favorable results of the Public Health Emergency Medical Countermeasure Enterprise-sponsored clinical study conducted by the Department of Defense evaluating the efficacy of Midazolam as compared to Diazepam as an anti-convulsive drug informed this solicitation. BARDA expected proposals for this medical countermeasure, which would replace Diazepam in existing CHEMPAKS, after 2012.

The Tables below outline cumulatively PBS acquisition contracts and solicitations that were initiated, completed, or continued in 2012, as well as new solicitations under PBS and the re-issuance of the CBRN Broad Agency Announcement for advanced research and development.

Table 1: Project BioShield Acquisition Contracts

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2012	Total Funding (Millions)	Reason for Use of Authority
Anthrax Therapeutics						
Monoclonal Antibody (Raxibacumab®, formerly Abthrax))	9/2005 (Base)	Completed (2008)	HGS	20,000 doses delivered; NDA filed with FDA (2008) & additional studies required by FDA (2009)	$174	Raxibacumab is an antitoxin used to treat anthrax and, along with vaccines and antibiotics, is part of a three-pronged approach taken by the U.S. Government to prepare for and respond to an anthrax attack. $8M was added to the contract to support studies required by the FDA.
	7/2009 (Option)	Ongoing	HGS	45,000 doses delivered of 45,000 contracted	$152 (2009) $8 (2011)	
Anthrax Immune Globulin (AIG)	9/2005 (Base)	Completed (2011)	Cangene	10,000 doses delivered	$144 (2011) $16.6 (2012)	AIG® is an antitoxin used to treat anthrax and, along with vaccines and antibiotics, is part of a three-pronged approach taken by the U.S. Government to prepare for and respond to an anthrax attack.
Anthrax Vaccines						
AVA (BioThrax®, Anthrax Vaccine Absorbed)	5/2005	Completed (2006)	Emergent (formerly BioPort)	10 million doses delivered	$243	BioThrax® is the U.S.-licensed vaccine for anthrax and, along with antitoxins and antibiotics, is part of a three-pronged approach taken by the U.S. Government to prepare for and respond to an anthrax attack.
AVA (BioThrax®, Anthrax Vaccine Absorbed)	9/2007	Completed (2008)	Emergent	18.75 million doses delivered	$448 (2008) $8.7 (2012)	
rPA (Recombinant Protective Antigen)	11/2004	N/A	VaxGen	Terminated 12/19/05	$2	Contract terminated
Botulism Therapeutics						
Botulinum Antitoxin (hBAT) Therapeutic	9/2006	Ongoing	Cangene	138,749 doses delivered of 200,000 contracted In addition plasma was delivered under the new contract modification	$415 (2006) $61 (2011)	Equine-derived polyclonal sera to multiple strains of (A-G) of *C. botulinum* used as a therapeutic for botulism. Reevaluation of the requirement led to a decrease in the number of doses necessary in the SNS. Thus, HHS/BARDA has met the requirement. The contract was modified and $61 M in additional funds were added to maintain the horse herd, stockpile plasma and continue stability testing of plasma and product in the SNS. This contract modification will ensure preparedness out to 2026.

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Table 1: Project BioShield Acquisition Contracts *continued from page 5*

Countermeasure Area/Product	Date of Contract Award	Delivery to Strategic National Stockpile	Contract Recipient	Status at the Close of CY 2012	Total Funding (Millions)	Reason for Use of Authority
Smallpox Vaccine						
Imvamune® MVA, (Modified Vaccinia Ankara) Smallpox Vaccine	6/2007	Ongoing	Bavarian Nordic	14.1 million delivered of 20 million contracted	$505 (2007) $37 (2012)	Imvamune® is an attenuated smallpox vaccine designated for immunocompromised persons as part of the overall strategy using vaccines and antiviral drugs for preparedness to and response to a smallpox *attack*.
Smallpox Antivirals						
ST-246	5/2011	TBD	SIGA Tech. Inc.	0 out of 1.7 M treatment courses (Deliveries begin March 2013)	$433	The SNS formulary currently contains smallpox vaccine for the general population, smallpox vaccine for immunocompromised individuals and vaccinia immune globulin (VIG) to treat adverse reactions to the vaccine for the general population. ST-246 will be used to treat those individuals who are symptomatic with disease; for which the vaccine has no efficacy. Late stage development and procurement of this drug complements the HHS formulary of MCMs to provide an appropriate response after a smallpox incident. In addition, this contract works toward the USG goal of developing two smallpox antivirals.
Medical Countermeasures for Radiological, Nuclear, and Chemical Threats						
Potassium Iodide (Thyroshield)	3/2005	Complete	Fleming	4.8 million doses, deliveries complete	$18	Provides capability for pediatric treatment
IV Calcium/Zinc DTPA (Diethylene triamine pentaacetic acid)	12/2005	Complete	Akorn	473,710 doses, deliveries complete	$22	Decorporation agent for radio-nuclear treatment

Table 2: Project BioShield ARD Solicitations

Name	URL	Pre-solicitation	Draft Solicitation	Final Solicitation	Closing Date	Expected Award Date	Reason for Use of Authority
CBRN MCM Development - BAA-CBNR-BAA-12-100-SOL-00011 "Rolling BAA"	https://www.fbo.gov/index?s=opportunity&mode=form&id=045ee83b87a8e95743fd68bb50e9e5a4&tab=core&_cview=1	2/2012	N/A	6/2012	Open Continuous Until 6/2013	N/A	N/A
RFP-12-100-SOL-00026 PBS Solicitation for Anthrax Antitoxins	https://www.fbo.gov/index?s=opportunity&mode=form&id=330fa7f5f757b0222f8bae5949a2674a&tab=core&_cview=1	6/2012	N/A	6/2012	8/2012	5/2012	Maintain Strategic National Stockpiles (SNS) at current preparedness to 2018 and maintain manufacturing capacity and capability established under the previous PBS contracts
RFP-12-100-SOL-00016 PBS Solicitation for Cytokines for Neutropenia Associated with ARS	https://www.fbo.gov/index?s=opportunity&mode=form&id=9d7557f75be7264e2b3a51101297edf7&tab=core&_cview=1	6/2012	N/A	8/2012	10/2012	6/2013	Increase preparedness against nuclear threats by including cytokines to treat acute radiation syndrome (ARS) in the SNS
RFP-13-100-SOL-00002 Solicitation notice for midazolam as a medical countermeasure for organophosphorus compound exposureorganophosphorus compound exposure	https://www.fbo.gov/index?s=opportunity&mode=form&id=53a1b9218d4e99274bdd82bcbaf18ce0&tab=core&_cview=0	11/2012	12/2012	12/2012	2/2013	7/2013	Replace current antidote contained in ChemPaks with a better product. Product can also be used in pediatric populations

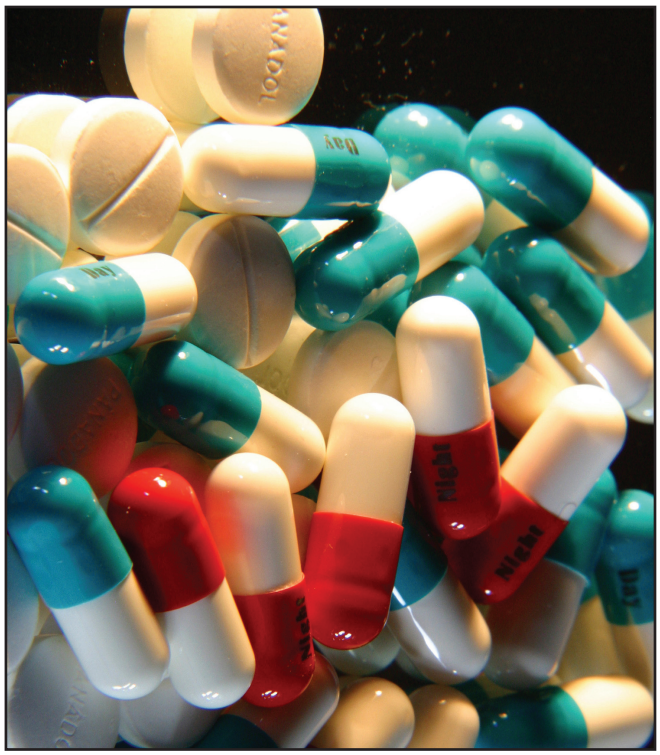
1.4 EMERGENCY USE AUTHORIZATION

Statutory Authority

In a public health emergency, potentially useful products may be available, but are not yet approved by the FDA for the particular use contemplated. Section 564 of the Federal Food, Drug, and Cosmetic (FD&C) Act (21 U.S.C. 360bbb-3), as amended by section 4 of the Project BioShield Act of 2004, permits the FDA Commissioner to issue an Emergency Use Authorization (EUA) to authorize the use of an unapproved medical product, or to authorize an unapproved use of an approved medical product, during an emergency declared by the HHS Secretary justifying the authorization. Such an emergency declaration may be issued based on a determination (a) by the Secretary of Homeland Security of a domestic emergency or a significant potential for a domestic emergency involving a heightened risk of attack with a specified CBRN agent; (b) by the Secretary of Defense of a military emergency or a significant potential for a military emergency involving a heightened risk to U.S. military forces of attack with a specified CBRN agent;[2] or (c) by the HHS Secretary of a public health emergency that affects or has a significant potential to affect national security and that involves a specified CBRN agent or a specified disease or condition that may be attributable to such agent or agents.[2] On July 26, 2007, FDA published a guidance document on FDA's policies for authorizing the emergency use of medical products under section 564 of the (FD&C) Act.[3]

Anthrax Preparedness

On July 20, 2012, the Secretary of HHS renewed the declaration, originally issued in 2008, justifying the authorization of the emergency use of all oral formulations of doxycycline accompanied by emergency use information for post-exposure prophylaxis of inhalational anthrax.[4]



During the 2012 reporting period, there were two EUAs in effect, both of which were issued in 2011 and subject to reporting during the 2011 reporting period. FDA issued these EUAs to facilitate pre-event planning, stockpiling, and preparedness efforts, including federal agency activities occurring under Executive Order 13527.[5] Both EUAs authorize certain unapproved uses of the antimicrobial drug doxycycline for post-exposure prophylaxis of inhalational anthrax in the event of a public health emergency involving B. anthracis, the biological agent that causes anthrax disease. The first EUA, issued on July 21, 2011, authorizes the use of all approved oral formulations of doxycycline products, including capsule, tablet, and liquid, where not contraindicated, for the post-exposure prophylaxis of inhalational anthrax.[6] The EUA allows certain aspects of emergency distribution, dispensing, and use of oral formulations of doxycycline products, which

[2]Pursuant to section 903 of the FD&C Act and existing delegations of authority, codified at 21 CFR part 5, the Secretary has delegated the authority to issue an EUA under section 564 to the FDA Commissioner. The text accurately describes the law as it existed in 2012, the time period covered by this report. As noted above, PAHPRA amended the FD&C Act to change this authority and add new emergency use authorities.

[3]http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm; See Notice in the *Federal Register*: 73 Fed. Reg. 62,507 (Oct. 21, 2008).

[4]Declaration of Emergency Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360bbb-3(b) (Oct. 1, 2008); renewed October 1, 2009 (74 Fed. Reg. 51,279) (Oct. 6, 2009); renewed October 1, 2010 (75 Fed. Reg. 61,489) (Oct. 5, 2010); renewed July 20, 2011 (76 Fed. Reg. 44,926) (July 27, 2011); renewal effective July 20, 2012 (77 Fed.Reg. 40,060)(July 6, 2012).

[4]Declaration of Emergency Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 360bbb-3(b) (Oct. 1, 2008); renewed October 1, 2009 (74 Fed. Reg. 51,279) (Oct. 6, 2009); renewed October 1, 2010 (75 Fed. Reg. 61,489) (Oct. 5, 2010); renewed July 20, 2011 (76 Fed. Reg. 44,926) (July 27, 2011); renewal effective July 20, 2012 (77 Fed.Reg. 40,060)(July 6, 2012).

[5]http://edocket.access.gpo.gov/2010/pdf/2010-38.pdf.

[6]*Authorization of Emergency Use of Oral Formulations of Doxycycline; Availability*, 76 Fed. Reg. 47,197 (Aug. 4, 2011).

would otherwise violate FDA's legal interpretations of the FD&C Act. The EUA allows public health authorities to stockpile doxycycline, so that, in the event of an anthrax emergency, they could mass dispense the authorized drugs with emergency use information and without individual prescriptions.

The second EUA, amended on October 14, 2011, was originally issued in 2008. As described in the previous four BioShield Annual Reports, FDA originally issued this EUA for the prepositioning of doxycycline hyclate tablet emergency kits for inhalational anthrax with United States Postal Service (USPS) participants and their household members as part of the Cities Readiness Initiative. The USPS EUA (now referred to as the National Postal Model) authorizes doxycycline hyclate tablet emergency kits to be distributed to and stored by eligible USPS employee volunteers and their household members. This program ensures that participants are ready at the outset of an emergency to distribute post-exposure prophylaxis to the affected population. The EUA has been amended three times to accommodate programmatic and operational changes and updates.[7]

FDA Pre-emergency Activities

As part of emergency preparedness activities, FDA continues to review and provide feedback on *pre-EUA* submissions for multiple products across all medical product lines.

[7] *Amended Authorization of Emergency Use Doxycycline Hyclate Tablet Emergency Kits for Eligible United States Postal Service Participants and Their Household Members; Availability*, 76 Fed. Reg/ 72,935 (Nov. 28, 2011).

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